

# Efficacy and Safety of Pralsetinib in Chinese Patients with Advanced RET Fusion+ Non-Small Cell Lung Cancer

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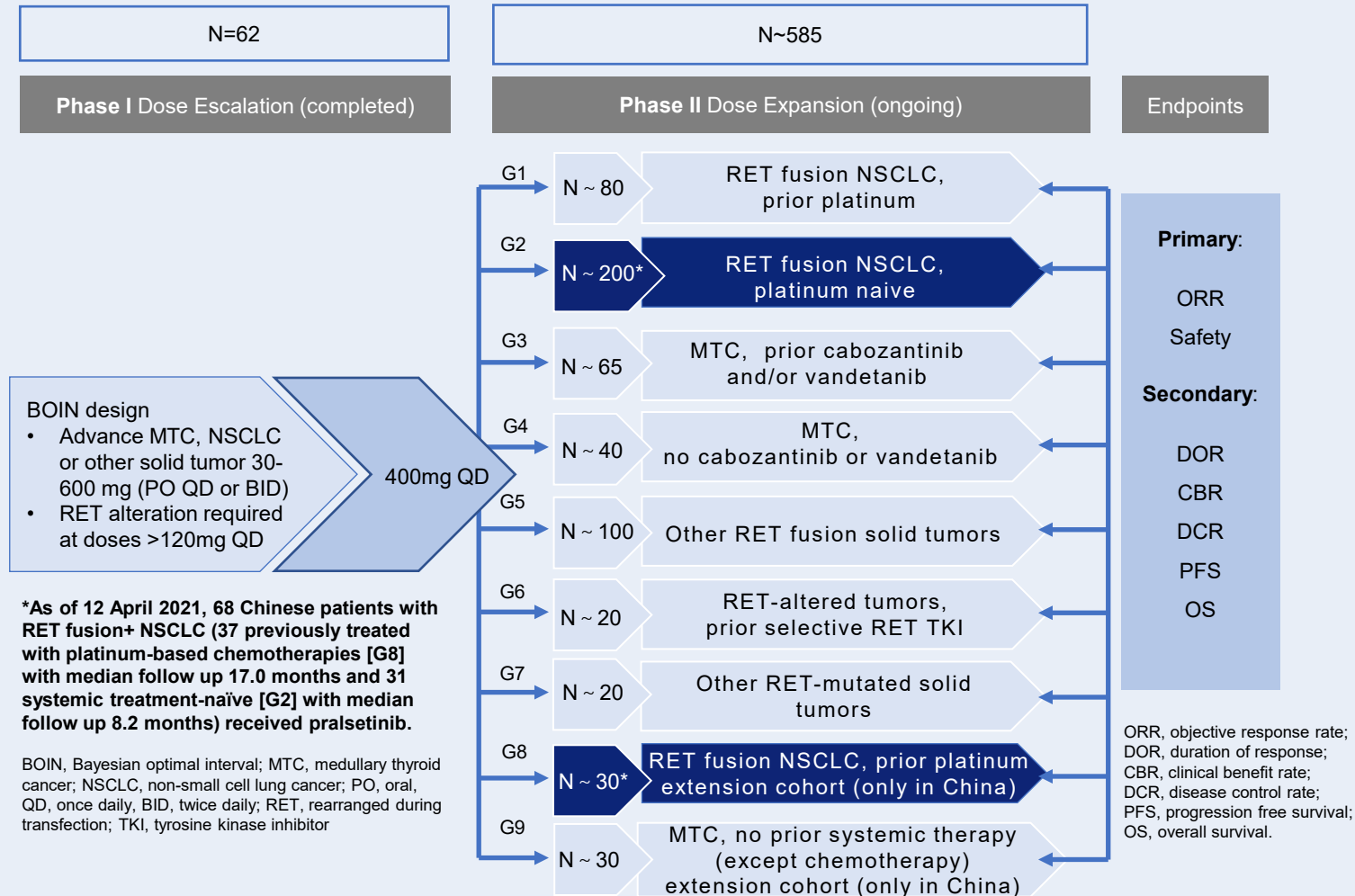
## Disclosure Information of Prof. Qing Zhou

Ineligible Company	Relationship(s)
AstraZeneca, Roche	Honorarium received from promotional activities

# 1 Background

- RET fusions have been reported as oncogenic drivers in approximately 1% to 2% of non-small cell lung cancer (NSCLC) patients<sup>1-4</sup>.
- Pralsetinib is a highly potent and selective rearranged-during-transfection (RET) kinase inhibitor targeting oncogenic RET alterations, including RET fusions<sup>5-6</sup>.
- U.S. FDA granted accelerated approval to pralsetinib in 2020 for the treatment of adults with metastatic RET fusion+ NSCLC and patients with advanced RET fusion+ thyroid cancer and RET-mutant medullary thyroid cancer.
- China NMPA approved pralsetinib in 2021 for the treatment of adults with locally advanced or metastatic RET fusion+ NSCLC who previously received platinum-based chemotherapy.
- A global phase I/II study “ARROW” (BLU-667-1101; NCT03037385) has showed broad and durable antitumor activity of pralsetinib in a variety of advanced RET-altered solid tumors, including RET fusion+ NSCLC.
- The primary analysis reported at WCLC 2020 has shown that pralsetinib provides rapid, durable tumor responses, and shows a well-tolerated safety profile in a cohort of Chinese patients with RET fusion+ NSCLC who received prior platinum-based chemotherapy.
- Here we present the efficacy and safety results of pralsetinib in both treated and treatment-naïve Chinese patients with RET fusion+ NSCLC.

# 2 ARROW Study Design



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**Data cut-off: April 12, 2021**

# Demographics and Baseline Characteristics

Characteristic	NSCLC patients in Chinese cohort	
	Prior platinum treatment (n=37)	No prior systemic treatment (n=31)
<b>Age, years, median (range)</b>	54 (26,77)	57 (30,79)
<b>Sex, male, n (%)</b>	17 (46)	11 (35.5)
<b>Race, Asian, n (%)</b>	37 (100)	31 (100)
<b>ECOG performance status, n (%)</b>		
0	2 (5.4)	1 (3.2)
1	35 (94.6)	30 (96.8)
<b>Histology type, n (%)</b>		
Adenocarcinoma	36 (97.3)	31 (100)
Other	1 (2.7)	0
<b>CNS metastasis, n (%)</b>	15 (40.5)	8 (25.8)
<b>Tumour stage at screening, n (%)</b>		
Stage IIIB	0	1 (3.2)
Stage IIIC	0	1 (3.2)
Stage IVA	8 (21.6)	12 (38.7)
Stage IVB	29 (78.4)	17 (54.8)
<b>Number of prior regimens, n (%)</b>		
1	14 (37.8)	0
2	5 (13.5)	0
≥3	18 (48.6)	0
<b>Smoking history, n (%)</b>		
Never smoked	25 (67.6)	21 (67.7)
Former	11 (29.7)	10 (32.3)
Current	1 (2.7)	0
<b>RET – Fusion Partner, n (%)</b>		
KIF5B	23 (62.2)	22 (71.0)
CCDC6	7 (18.9)	5 (16.1)
Other	7 (18.9)	4 (12.9)

ECOG, Eastern Cooperative Oncology Group;  
CNS, Central Nervous System;  
RET, rearranged during transfection;

**Data cut-off: April 12, 2021**

# Efficacy Summary

**Pralsetinib demonstrated robust anti-tumor activities in RET fusion+ NSCLC patients regardless of prior therapies**

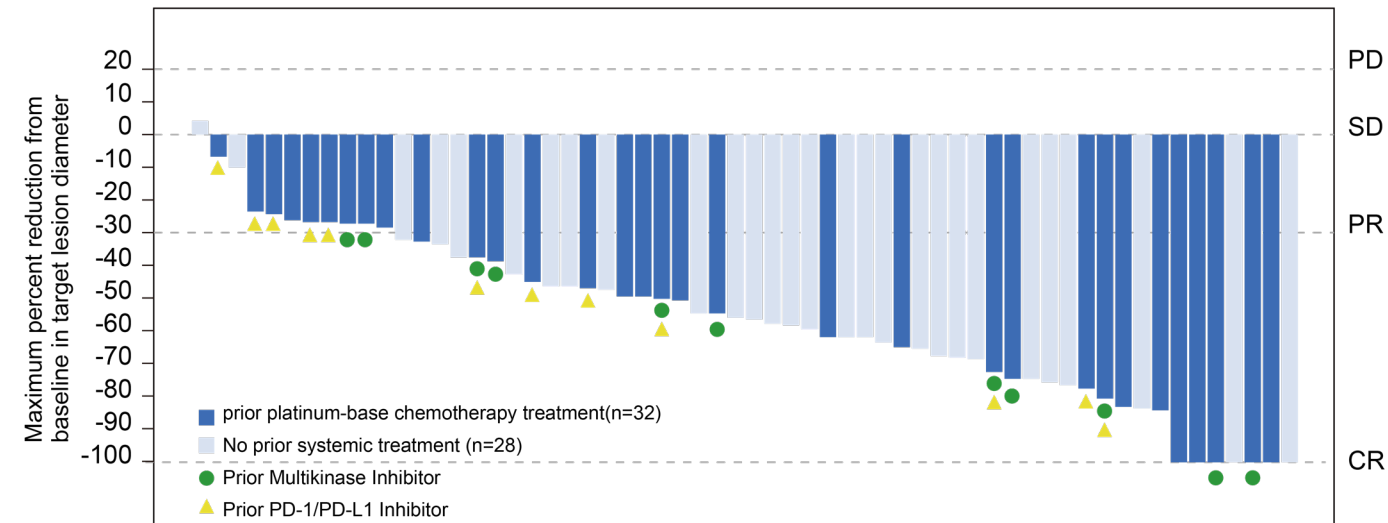
## Response Summary of Patients with Measurable Baseline Disease per BICR

Outcome	NSCLC patients in Chinese cohort	
	Prior platinum-based chemotherapy treatment (n=33)	No prior systemic treatment (n=30)
<b>Confirmed ORR, n(%) [95% CI]</b>	22 (66.7) [48.2-82.0]	24 (80.0) [61.4-92.3]
<b>CR, n(%)</b>	1 (3.0)	2 (6.7)
<b>PR, n(%)</b>	21 (63.6)	22 (73.3)
<b>SD, n(%)</b>	9 (27.3)	2 (6.7)
<b>PD, n(%)</b>	1 (3.0)	2 (6.7)
<b>NE, n(%)</b>	1 (3.0)	2 (6.7)
<b>*CBR, % (95% CI)</b>	84.8 (68.1-94.9)	86.7 (69.3-96.2)
<b>DCR, % (95% CI)</b>	93.9 (79.8-99.3)	86.7 (69.3-96.2)

\*Confirmed CR, PR or SD  $\geq$ 16 Weeks

BICR, Blinded Independent Centralized Review; ORR, objective response rate; CI, confidence interval; CR, complete response; PR, partial response; SD, stable disease; PD, progress of disease; NE, not evaluable; CBR, clinical benefit rate; DCR, disease control rate;

## Maximum Tumor Shrinkage in Target Lesion (N=60\*\*)



\*\* 3 patients were not included due to absence of evaluable post-baseline disease response assessment by BICR per RECIST v1.1

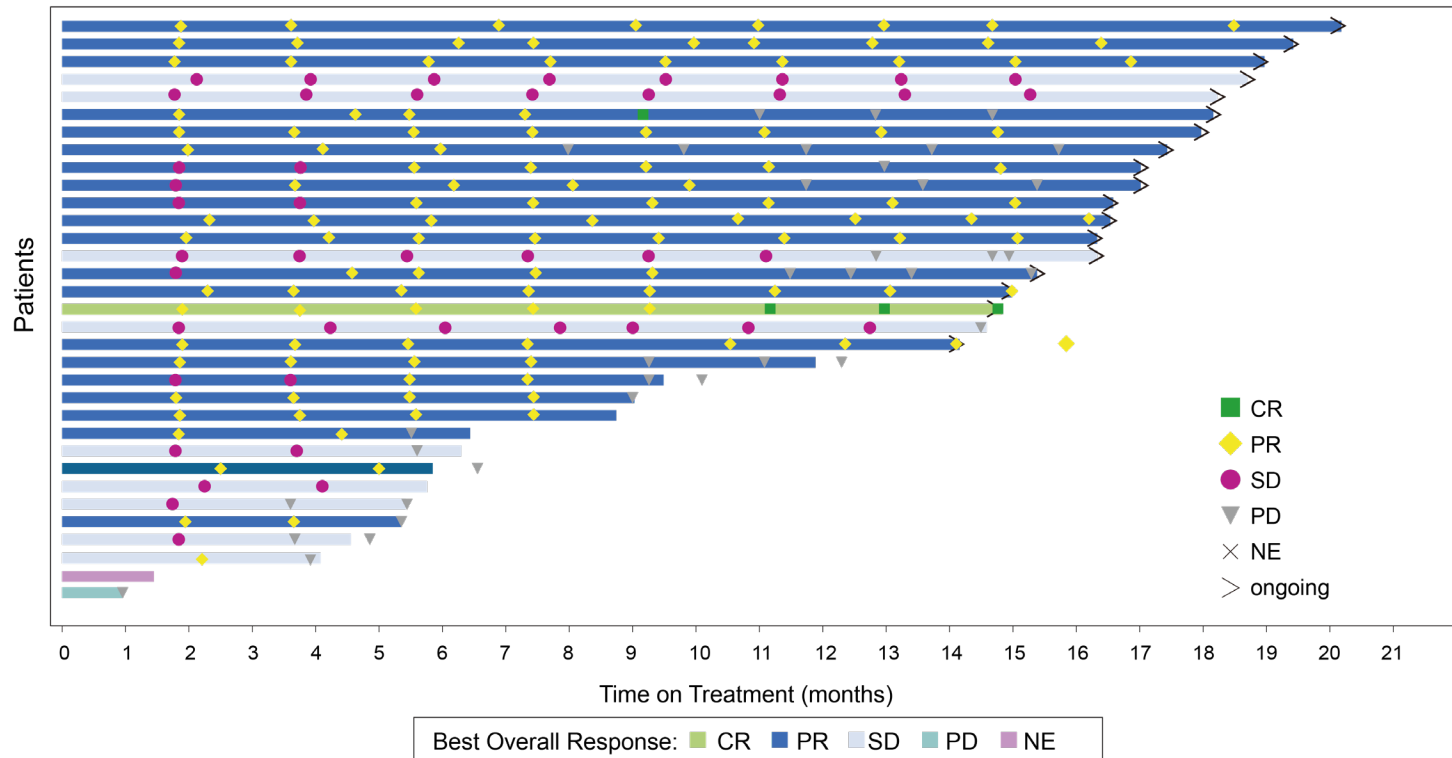
PD, progress of disease; SD, stable disease; PR, partial response; CR, complete response.

Data cut-off: April 12, 2021

# Efficacy Summary

## Pralsetinib induces rapid and durable response in RET fusion+ advanced NSCLC in Chinese cohort

### Group 8 (NSCLC after prior platinum-based chemotherapy): Duration of Treatment and Response (N=33)



CR, complete response; PR, partial response; SD, stable disease; NE, not evaluable;

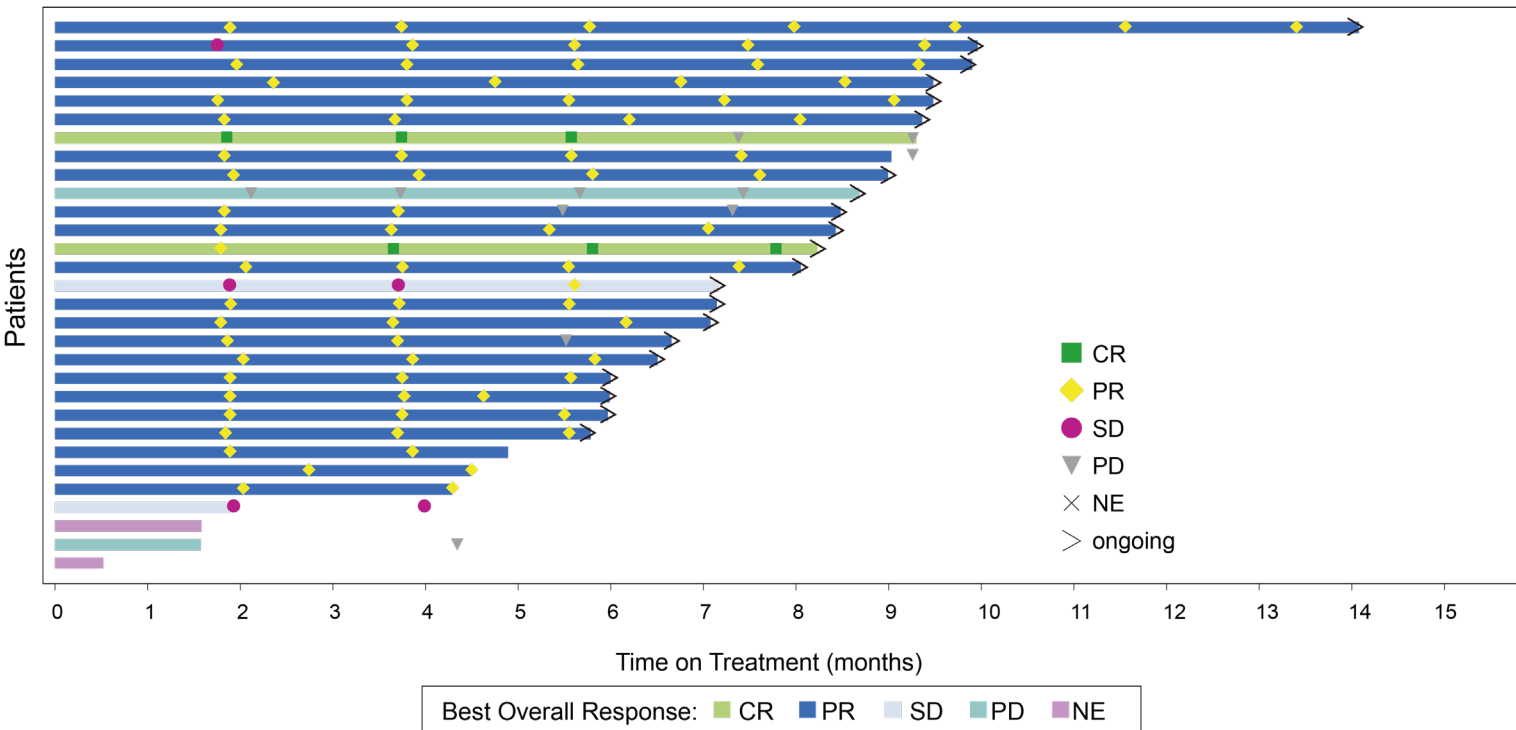
- Median follow up was 17.0 (range: 16.3-18.1) months.
- Median treatment duration was 14.65 (range: 0.9-20.0) months.
- 68.18% (15/22) of responders remain on treatment.
- Median time to first response among the 22 responders was 1.89 (1.7-5.6) months.
- 6-month and 9-month DOR rates were 77.3% (95% CI: 59.8-94.8) and 50.0% (95% CI: 29.1-70.9), respectively.

Data cut-off: April 12, 2021

# Efficacy Summary

## Pralsetinib induces rapid and durable response in RET fusion+ advanced NSCLC in Chinese cohort

### Group 2 (treatment-naive NSCLC): Duration of Treatment and Response (N=30)



CR, complete response; PR, partial response; SD, stable disease; NE, not evaluable;

- Median follow up was 8.2 (range: 7.1-8.6) months.
- Median treatment duration was 7.13 (range: 0.5-14.0) months.
- 79.17% (19/24) of responders remain on treatment.
- Median time to first response among the 24 responders was 1.87 (1.7-3.8) months.
- 6-month and 9-month DOR rates were 76.7% (95% CI: 55.6-97.8) and 38.3% (95% CI: 0.0-92.5), respectively.

Data cut-off: April 12, 2021

# Safety Overview

**Pralsetinib well tolerated in Chinese patients with RET fusion+ NSCLC with a manageable safety profile**

## Treatment-Related AEs in $\geq 20\%$ of Patients

Preferred Term	Overall (N=68)	
	Any grade, n (%)	Grade 3-4, n (%)
Aspartate aminotransferase increased	55 (80.9)	3 (4.4)
Neutrophil count decreased	54 (79.4)	23 (33.8)
Anaemia	46 (67.6)	22 (32.4)
White blood cell count decreased	41 (60.3)	9 (13.2)
Alanine aminotransferase increased	39 (57.4)	3 (4.4)
Blood creatine phosphokinase increased	31 (45.6)	12 (17.6)
Hypertension	24 (35.3)	8 (11.8)
Platelet count decreased	21 (30.9)	6 (8.8)
Blood creatinine increased	20 (29.4)	1 (1.5)
Bilirubin conjugated increased	19 (27.9)	0
Constipation	19 (27.9)	0
Gamma-glutamyltransferase increased	19 (27.9)	4 (5.9)
Blood alkaline phosphatase increased	18 (26.5)	2 (2.9)
Malaise	17 (25.0)	0
Blood bilirubin increased	16 (23.5)	1 (1.5)
Hypocalcaemia	14 (20.6)	1 (1.5)

- All 68 patients experienced at least one treatment emergent adverse event
- 67/68 (98.5%) patients experienced treatment-related adverse events (TRAEs).
- 7/68 (10.3%) patients discontinued from treatment due to TRAE.

### Additional Grade 3-4 TRAEs( $\geq 5\%$ ):

- Lymphocyte count decreased (5.9%)
- Leukopenia (5.9%)
- Hypophosphataemia (11.8%)

Data cut-off: April 12, 2021



# Conclusions

- Pralsetinib is a promising targeted therapy with rapid and durable clinical activity in Chinese patients with RET fusion+ NSCLC regardless of prior therapies.
- Efficacy results observed in Chinese population are consistent with those previously reported from the global population in the ARROW trial.
- Pralsetinib safety profile in Chinese patients is manageable, with no new safety signals detected.
- Pralsetinib, with a favorable benefit-risk profile, represents an efficacious treatment option and demonstrates the potential of being a new Standard-of-Care to Chinese patients with RET-fusion driven advanced NSCLC.

Data cut-off: April 12, 2021

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